## Remarks

Amendments to the Claims

Claims 2, 27, and 28 are amended to recite "if it modulates the activity of the pDE10A polypeptide." The specification supports this amendment on page 43, lines 18-19.

Claim 28 is amended to recite liver diseases, diabetes, and kidney diseases. The specification supports these amendments on page 60, lines 1-18 (liver diseases), page 61, line 16 to page 62, line 22 (diabetes), and page 69, lines 10-16.

The amendments do not add new matter.

Rejection of Claims 2 and 28 Under 35 U.S.C. § 102(b)

Claims 2 and 28 stand rejected under 35 U.S.C. § 102(b) as anticipated by Fujishige.[1] Applicants respectfully traverse the rejection.

To determine whether a claim is anticipated by a prior art reference, one must first recognize each element of the invention recited in the claim and determine whether the prior art reference discloses the same element(s). *Kalman v. Kimberly-Clark Corp.*, 218 U.S.P.Q. 781, 789 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). One must then determine whether the prior art reference describes the invention sufficiently so that one of skill in the art could make the invention. *In re LeGrice*, 133 U.S.P.Q. 365, 373-74 (C.C.P.A. 1962).

The Office Action contends that Fujishige anticipates claims 2 and 28 "because the only nexus between PDE10A and various diseases claimed [sic; disclosed] in the specification is the tissue specific expression patterns which is shown by Fujishige in Fig. 3 on page 18442." Office

[1] Fujishige *et al.*, *J. Biol. Chem. 274*, 18438-45, 1999.

Action at page 3 lines 2-4. Fujishige, however, does not teach the expression patterns disclosed in the present specification.

Claim 2

Claim 2 is directed to a method of screening for therapeutic agents useful in the treatment of a cardiovascular disease. As Applicants explained in the response filed December 7, 2006, Fujishige does not expressly or inherently describe identifying a test compound as a potential therapeutic agent useful in the treatment of a cardiovascular disease as recited in claim 2 as amended. Nor does the expression data reported in Fujishige permit one skilled in the art to conclude that a test compound could be a useful therapeutic agent for treating a cardiovascular disease. The expression data shown in Fujishige's Figure 3 indicates a relatively low expression of PDE10A mRNA in the heart. Expression in the heart is not mentioned in either the Results or the Discussion sections of Fujishige. There is nothing in Fujishige's text or data which teaches or suggests that PDE10A would be a useful target for treating any cardiovascular disease.

In contrast, Applicants' specification teaches that PDE10A is differentially expressed between sclerotic aorta and normal aorta and between sclerotic coronary artery and normal coronary artery. See page 92. Fujishige does not teach or suggest this differential expression.

Claim 28

Claim 2 is directed to a method of screening for therapeutic agents useful in the treatment of Alzheimer's disease. There is no expression pattern disclosed in Fujishige which teaches or suggests an association of PDE10A with Alzheimer's disease. Fujishige teaches modest expression of PDE10A in "brain," which reflects the average of the expression in the whole brain. Fujishige also teaches high expression in the putamen and caudate nucleus, which Fujishige states indicates the possibility of genetic linkage of the PDE10A gene with juvenile

Parkinson's disease. Page 18445, col. 1, first full paragraph. High expression in the putamen and caudate nucleus, however, does not teach or suggest an association of PDE10A with Alzheimer's disease.

In contrast, Applicants' specification teaches that PDE10A is differentially expressed between normal cerebral cortex and the cerebral cortex in Alzheimer's disease. See page 93. Fujishige does not teach or suggest this differential expression.

Fujishige does not anticipate either claim 2 or claim 28. Please withdraw the rejection.

Rejection of Claims 2, 27, and 28 Under 35 U.S.C. § 103(a)

Claims 2, 27, and 28 stand rejected under 35 U.S.C. § 103(a) as obvious over Fuishige. Applicants respectfully traverse the rejection.

The U.S. Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of obviousness. The *prima facie* case requires three elements:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

M.P.E.P., 8th ed., § 2142. The Office Action has not made a *prima facie* case that any of claims 2, 27, and 28 is obvious. Fujishige does not teach all the elements of claims 2, 27, and 28 and does not suggest to the ordinary artisan any modification which would result in the methods to which these claims are directed.

In determining whether a claimed invention is *prima facie* obvious, the teachings of a cited reference must be considered as a whole and compared with the subject matter of the

rejected claims. *Graham v. John Deere* 383 U.S. 1, 17 (1966). Fujishige demonstrates PDE10A mRNA expression in various tissues and contains the following observations about that expression:

> PDE10A transcripts were particularly abundant in the putamen and caudate nucleus regions of brain and [in] testis. Moderate expression was observed in the thyroid gland, pituitary gland, thalamus, and cerebellum.
>
> * * *
>
> The localization of PDE10A transcripts in the brain is of interest . . . . PDE10A is expressed in the putamen and caudate nucleus regions that have dopamine receptors and are related to juvenile parkinsonism. Thus, the possibility of genetic linkage of the PDE10A gene with this disease is intriguing.

Fujishige at page 18442, col. 2, lines 5-8; page 18444, col. 2, line 24 to page 18445, col. 1, line 16. As discussed above, there is absolutely nothing in Fujishige which teaches or suggests that PDE10A is associated with cardiovascular disease (as recited in claim 2) or with Alzheimer's disease (as recited in claim 28). In contrast to the present specification, there is also nothing in Fujishige which teaches or suggests that PDE10A is associated with cancer, liver diseases, diabetes, or kidney disease as recited in amended claim 27:

- The present specification teaches differential expression of PDE10A mRNA between normal tissues and corresponding tumors (see pages 92-94); Fujishige does not examine PDE10A mRNA expression in any tumors.
- The present specification teaches differential expression of PDE10A mRNA between normal liver and cirrhotic liver (page 92); there is no detectable PDE10A mRNA expression in the liver in Fujishige's Figure 3, and Fujishige did not examine any diseased liver tissue.

- The present specification teaches expression of PDE10A mRNA in the pancreas (page 92); there is no detectable PDE10A mRNA expression in the pancreas in Fujishige's Figure 3.
- The present specification teaches high expression of PDE10A mRNA in the kidney (page 94); Fujishige's Figure 3 demonstrates only modest expression in the kidney (not rising to the level of the "moderate expression" Fujishige describes in the thyroid gland, pituitary gland, thalamus, and cerebellum; see page 18442, col. 2, lines 6-8).

The Office Action contends that it would be obvious for one of ordinary skill to identify compounds as potential therapeutic agents "useful in the treatment of many diseases" merely because Fujishige suggests a link between a tissue-specific pattern of PDE10A mRNA expression and juvenile parkinsonism. Paragraph bridging pages 3 and 4 of the Office Action. This is a leap which the ordinary artisan would not have made.

The Office Action has not made a *prima facie* case of obviousness. Please withdraw the rejection.

Respectfully submitted,

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Dated: January 8, 2008

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